REMARKS/ARGUMENTS

Present Invention and Pending Claims

Claims 19-22 and 31-45 are pending and directed to a compound (claims 19 and 20), a composition (claims 21 and 22), a method of inhibiting CETP activity in a patient (claim 31), a method of increasing HDL in a patient (claim 32), a method of treating or preventing atherosclerosis in a patient (claim 33), a method of treating or preventing hyperlipidemia in a patient (claim 34), and methods of preparing a compound of formula (1) (claims 35-45).

Summary of the Claim Amendments

Claims 23-30 have been canceled, and claims 1-18 had been canceled previously. The phrase "hydrates, and solvates" has been deleted from claims 19 and 21. No new matter has been added by way of these amendments.

Summary of the Office Action

Claims 19 and 21 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Claims 23-34 also have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Claims 35-45 have been deemed allowable. Claims 20 and 22 have been objected to as being dependent on a rejected base claim, but otherwise would be found allowable. Reconsideration of the pending claims is hereby requested.

Discussion of the Enablement Rejection of Claims 19 and 21

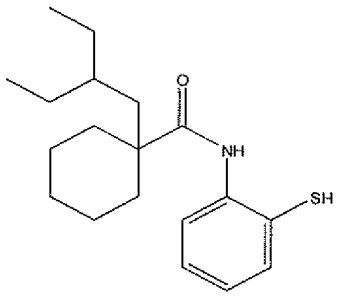
According to the Office Action, claims 19 and 21 lack enablement because of the terms "hydrates" and "solvates." Claims 19 and 21 have been amended to delete the terms "hydrates" and "solvates." Accordingly, this rejection has been rendered moot.

Discussion of the Enablement Rejection of Claims 23-34

Claims 23-34 allegedly are not enabled because the specification does not provide guidance regarding any special method of administration that would be required to deliver the claimed compound so that it would be efficacious *in vivo*.

In order to advance prosecution, claims 23-30 have been canceled. With respect to claims 31-34, the enablement rejection is traversed based on the following remarks.

As pointed out by the Examiner, the therapeutic activity of the compound recited in claims 31-34 has been reported in post-filing publications (Office Action, page 4). Also as pointed out by the Examiner and the cited references, the thiol compound recited in the pending claims, while readily synthesized and administerable, is generally unstable (see, for example, Okamoto et al., *Nature*, 406: 203-207 (July 2000), page 204, left column, second full paragraph). To contend with the stability issues of the highly active thiol compound, orally bioavailable thioesters were prepared. As reported in Okamoto et al. (*supra*), thioester JTT-705 readily hydrolysed to the active thiol, i.e., the compound of the pending claims:



(page 204, left column, top paragraph). Okamoto et al. (*European Journal of Pharmacology*, 466: 147-154 (2003)) also reported that thioester "JTT-705 is hydrolyzed to the thiol form in plasma or neutral buffer, and the inhibitory activity of JTP-25203 [i.e., the compound of the pending claims] is superior to that of JTT-705 *in vitro*" (page 152, right column, "Discussion"). Thus, upon *in vivo* administration of a thioester, such as JTT-705, the thioester bond is cleaved, thereby forming the active thiol compound. The thiol compound recited in the pending claims has high activity and can, for example, inhibit CETP activity in a patient, increase HDL, treat or prevent atherosclerosis, and/or treat or prevent hyperlipidemia.

The present specification embodies administration of compounds that can form the thiol compound *in vivo*. See, for example, the paragraph bridging pages 32-33, which describes "Z" being a mercapto (-SH) protecting group. In particular, the specification describes mercapto-protecting groups that can dissociate *in vivo*, thereby forming the active thiol compound. For example, compound **26** ("JTT-705") has Z equal to $-C(O)CH(CH_3)_2$, which is an acyl group as defined by the specification. Ample description of administering

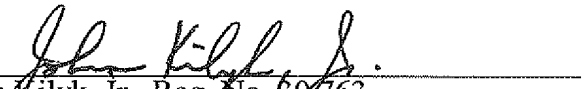
compounds comprising mercapto-protecting groups, including thioesters (e.g., compound **26**), also is provided. See, for example, Test Example 2 and Tables 38-48.

Given the teachings of the specification and literature and the evidence that the compound of the pending claims is highly potent as a CETP inhibitor, one of ordinary skill in the art would be able to use the methods recited in claims 31-34 without undue experimentation. As a result, the subject matter of claims 31-34 is fully enabled. Applicants respectfully request that, in view of the foregoing, this rejection be withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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